

AN ACCOUNT OF A FORM OF SPLENOMEGALY WITH HEPATIC CIRRHOSIS, ENDEMIC IN EGYPT

BY

H. B. DAY, M.D., B.S. (LOND.), M.R.C.P.,

MEDICAL TUTOR AND REGISTRAR, KASR-EL-AINY HOSPITAL, CAIRO,

AND

A. R. FERGUSON, M.D., C.M.,

PROFESSOR OF PATHOLOGY, GOVERNMENT SCHOOL OF MEDICINE, CAIRO.

(Received for publication 30 July, 1909)

INTRODUCTORY

All medical men who have had experience of native practice in Egypt are aware of the frequency of cases of ascites due to hepatic cirrhosis. Thus we find that such cases account for 4 per cent. of admissions to the medical wards of Kasr-el-Ainy Hospital, Cairo, as compared with 0.9 per cent. in the large London hospitals. This fact is striking, as it occurs in a country where the large majority of the inhabitants are Moslems and alcoholic excess is rare. Moreover, its prevalence in children, and peculiar clinical and pathological characters, easily distinguish it from the ordinary European variety.

Familiarity with the condition of the liver and spleen in such cases enables one to recognise the great prevalence of the disease in an earlier stage, before the onset of ascites. An enlargement of both these viscera is frequently noted in patients admitted for various complaints, and the liver may be felt in all stages of cirrhosis. Finally, it is a common experience to find splenic enlargement without obvious hepatic changes in patients who present no history nor signs of malarial infection.

The notorious difficulties of tracing hospital patients at home are as nothing compared with the impossibility of obtaining any reliable information whatever of the antecedent or subsequent histories of native patients seen in hospital. Only large experience

can partly remedy this defect, and the history and course of the disease must be gathered more from careful observation of patients admitted in various stages rather than from a series of individual cases followed from the commencement to the end.

GENERAL ETIOLOGY

Incidence. Hepatic cirrhosis must be considered one of the common diseases which affect the native Egyptian, although much less prevalent than trachoma, ankylostomiasis and bilharziosis. A census of native patients in the medical wards of Kasr-el-Ainy Hospital showed that over 4 per cent. were admitted for ascites, and no less than another 16 per cent. had the disease in easily recognisable form, while an additional 7 per cent. had chronic splenic enlargement which in most instances represented the earliest stage of the disease.

This cirrhosis frequently complicates ankylostomiasis and pellagra, and is especially common when these two diseases exist in combination. This association, while striking clinically, has little direct relationship, for advanced cases of both diseases generally show no signs of cirrhosis during life or at autopsy. Further, ankylostomiasis and pellagra are the two commonest diseases on the returns from the medical side.

A truer idea of the prevalence of the disease is afforded by the results of a special routine examination of all native patients admitted to the surgical and eye sections (septic cases excluded). Of a total of 300 of all ages :

8 per cent. had splenic enlargement (chronic).

3.3 per cent. had enlargement of the liver and spleen.

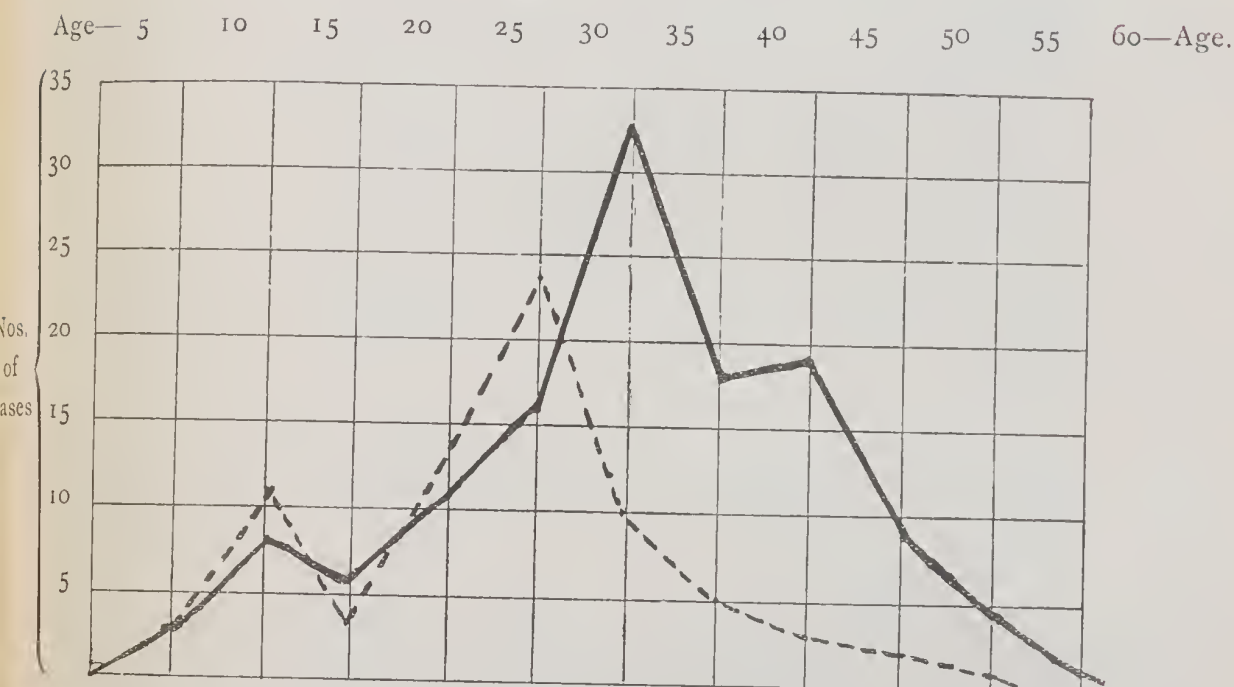
2.3 per cent. had definite cirrhosis with enlarged spleen.

This total is not large enough to show the incidence at each decade with accuracy, but the results so far bear out the age incidence recorded below. On this point an interesting investigation has already been begun by Dr. E. H. Ross, Medical Officer of Health for Cairo, who examined over 7,000 children under 16 years of age and found 6.8 per cent. with enlarged spleens.

Age. The appended chart shows the numbers and ages of cases admitted during two years, in two curves, the continuous line showing the age incidence among patients with well-established disease and

the interrupted the ages of those admitted with hepatic ascites. It will be seen on comparison that this disease is most common after twenty-five, and that the onset of ascites is generally postponed for five or more years. The irregularity of the fall in the latter group is probably due to the difficulty in estimating the age, as native patients are quite ignorant on this point.

CHART SHOWING AGE INCIDENCE



Sex. According to the above return the disease is equally prevalent in either sex. The special census of hospital patients showed a decided predominance in the male sections, but this may be explained by the small numbers of young female adults admitted of the age at which the disease is most common. A family history was rarely obtainable, but little reliance can be placed on such statements, which only special village investigation can establish or disprove.

SYMPTOMS

Although in its later stages this disease presents a characteristic picture, its onset is unattended by any constant symptom except a slow painless enlargement of the spleen. Upon examination this

organ is felt slightly enlarged, of a firmer consistence than normal, descending one or two finger-breadths below the costal margin on inspiration. Some degree of anaemia is the rule rather than the exception among the native population owing to the prevalence of ankylostomiasis, but is not a special feature of these cases.

Inquiry among patients in a later stage of the disease showed that no symptom other than abdominal enlargement and discomfort had been noticed in 55 per cent.; 29 per cent. described an onset with fever of an irregular type persisting a month or longer, while the remaining 16 per cent. dated their trouble from an attack of dysentery or prolonged diarrhoea. The exact significance of such intestinal disturbance is uncertain, but it must be remembered that amoebic dysentery is one of the commonest diseases of Egypt.

The second stage of the disease is indicated by definite hepatic involvement, with increased enlargement of the spleen, accompanied by local and general symptoms. The blood shows the special changes described in a later section. The clinical picture now presented is by no means identical in every patient, as will appear on comparison of the cases illustrated in the photos A, B and C. The following set of symptoms are, however, found in every case, although they may vary in intensity in different patients or at different times in the same patient.

(1) *Wasting*. In most patients the disease is suggested by their appearance. Instead of the extreme pallor with retention of fat which characterises ankylostomiasis, or the emaciation with localised pigmentation distinctive of pellagra, we find a moderate anaemia with more or less wasting. The combination of marked anaemia with wasting in an Egyptian generally indicates the co-existence of ankylostomiasis and cirrhosis.

(2) *Fever*. The great majority of cases show slight fever of an irregular type. In 63 per cent. this did not exceed 37·5, but in 28 per cent. there were excursions up to 38, and in 9 per cent. this temperature was exceeded. Occasionally patients may show high fever for some weeks due to an exacerbation of the disease itself and not to any complication. The temperature, as in Case C, may show a double remission in the twenty-four hours, similar to that described in Kala-azar.

(3) *Local symptoms and signs.* A dragging pain in the left side due to the enlarged spleen is common. Discomfort after meals and tenderness over the hypochondrium is generally present at some stage, caused by commencing perisplenitis and perihepatitis. In advanced cirrhosis, congestion of the stomach and fixation by adhesions may set up a chronic dyspepsia which the patient seeks to relieve by inducing vomiting after a heavy meal. Haematemesis is not common, but may be the first symptom of the disease and be accompanied by other signs of portal congestion. These complaints are often illustrated by the scars of cauteries, setons, etc., with which the patient has sought to relieve his pain. See photos A and D.

Upon examination the abdomen is seen to present the characteristic shape illustrated in Plates VIII, IX, X. There is an outward expansion of the lower ribs, a widening out of the costal angle, and a general enlargement of the upper part of the abdomen—often with separation of the recti muscles—the result of the pressure exerted by the enlargement of the liver and spleen, which may indeed form visible swellings.

The condition of these viscera varies within considerable limits, and is influenced by the duration and severity of the disease, and possibly also by the age of the patient. The liver is felt uniformly enlarged, smooth at first and of firmer consistence than normal. Later this enlargement is attended with fibrotic contraction which gives it an irregular granular surface. The largest liver noted in this stage measured six inches downwards from the costal margin in the nipple line. With increasing cirrhosis the organ shrinks, but is rarely reduced to less than its normal weight. When the spleen is much enlarged the hepatic changes are obscured, since this organ is displaced upwards and to the right.

The spleen attains its greatest dimensions when the disease is advancing rapidly, more especially in young subjects below the age of 20. Two illustrative cases are shown in Plates VIII and X. In such patients it may reach some distance beyond the umbilicus, and the diaphragm with the thoracic viscera are displaced upwards. It may overlap the liver if the latter be also much enlarged.

With the gradual development of hepatic cirrhosis the spleen becomes much harder and may shrink somewhat. Thus the state of the liver can generally be inferred from the consistence of the spleen,

for if the latter be hard, even if only projecting a finger breadth below the costal margin, hepatic changes are certain to be advanced. Adhesions may prevent the descent of the spleen, and in some cases, where the liver has been markedly cirrhotic, the former organ could not be felt on abdominal examination.

The duration of this stage may apparently be indefinite. The longest interval noted before the appearance of ascites was fifteen years. Many mild cases may show no further symptoms, and the progress of the disease be arrested or the patient be carried off by some intercurrent illness. (Plate XI.)

The disease, however, attracts most notice when the hepatic cirrhosis is followed by ascites with its attendant miseries. This serious event may be due to the gradual obliteration of hepatic vessels, but in many cases the history suggests that a fresh infection, acting on an already cirrhotic organ, may be responsible. Evidences of portal congestion, such as nausea, vomiting, haematemesis, melaena and haemorrhage from the bowel or from piles may precede its onset. Rapid emaciation follows.

At this stage the patient presents the familiar picture of cirrhotic ascites. (Plate XII.) The pinched features and wasted limbs offer a striking contrast to the greatly swollen abdomen. The effect of the high intra-abdominal pressure is seen in the protuberant umbilicus and network of dilated superficial veins which return blood from the oedematous legs into anastomoses with the thoracic vessels. Jaundice is rare except as a terminal event. Upon palpation the cirrhotic liver can usually be felt in the epigastric angle, and the enlarged spleen recognised by 'dipping.' Most cases with ascites require tapping on admission, and this has to be repeated on an average every ten days, about eight kilos being withdrawn on each occasion. After removal of the fluid these organs can be better investigated, when the liver is more often found enlarged than contracted, and the spleen hard and of considerable size. The heart is displaced upwards, the urine may show traces of albumen, and congestion of the bases of the lungs with bronchitis usually follows. These latter signs may be an indication of heart failure and be complicated by the development of hydrothorax.

The duration of this stage is considerably shorter, and may be reckoned in months instead of years; the consequent prognosis is

much the same as in the alcoholic variety. The records of fatal cases show that death occurred on an average four months after the appearance of ascites; the longest interval was four years. Occasionally one meets cases where the patient has been temporarily or permanently cured. Thus two patients were tapped and remained free from ascites for three and a half and twelve years respectively. A recurrence in the latter case proved fatal, and at the autopsy no sign of syphilitic disease was discovered. Operation omentopexy has not so far given encouraging results, perhaps owing to the advanced state of the disease at the time.

The immediate cause of death was commonly hepatic insufficiency, the patients gradually passing into a comatose state—occasionally with jaundice. Lung complications and heart failure from exhaustion account for most of the remainder.

PATHOLOGICAL ACCOUNT OF THE DISEASE

A disease, characterised as this is, by initial fever, a chronic course, and a group of symptoms referable to slowly progressive changes in the liver, with either concurrent or consecutive changes in the spleen, exhibits many points of resemblance to Kala-azar. We have accordingly, during the past four years, examined the blood, spleen-pulp, and liver tissue during life, from such cases as illustrated the many clinical features in typical fashion.

Before proceeding to summarise the results of these observations, it may at once be said that we have never found in material taken from spleen or liver any parasites with the characters of the Leishman-Donovan body.

The blood has been examined by us in upwards of forty cases. The majority of these were admitted to hospital for the relief of ascites, cirrhotic change in the liver with splenic enlargement being already well established. The degree of anaemia is sometimes extreme, only 1,330,000 red corpuscles per cubic mm. being recorded in one of our cases. The average number of red corpuscles per cubic mm. in the forty cases examined was 2,635,440. The red corpuscles exhibit very considerable variations in size in the more advanced stages of the disease, although the discoid form is usually preserved. Polychromatophilia is frequently observed, chiefly

affecting the larger corpuscles, but the occurrence of nucleated red corpuscles is a very rare phenomenon.

With regard to the white cells, a definite leucopenia has always been found during what may be called the 'hospital phase' of the disease. Thus, the average leucocyte count in the series of cases examined was 4,503 per cubic mm., and the percentage proportions of the main varieties of leucocytes present, calculated from a series of differential analyses, gives the following figures:—

Polymorphonuclear neutrophiles	62·84
Lymphocytes	25·26
Large lymphocytes and hyaline cells	5·50
Eosinophiles	6·40
	<hr/>
	100·00
	<hr/>

Mast-cells are usually present, but seldom exceed the normal limit of 0·5 per cent. Neutrophile myelocytes were noted in a small proportion of the cases, but never exceeded 0·5 per cent.; for the sake of simplicity, therefore, these two classes of cells have been omitted from the composite table. It will thus be seen that the polymorphonuclear cells are relatively diminished, while the proportions of the other classes, and particularly of the large hyaline cells and eosinophiles, are distinctly increased. A certain degree of eosinophilia is of such frequent occurrence in Egypt, as the result of Bilharzial or Ankylostomal infections, that this feature of the blood formula may be at once discounted.

The bone-marrow has always been found more or less profoundly affected. That of the ribs is almost always diffuent, its colour varying with the degree of anaemia. The femur always manifests an active transformation of its marrow; in some cases this is of a reddish gelatinous character, and in others it is of deep red colour and firm consistence, resembling in appearance that of pernicious anaemia. In both situations the hyaline non-granular elements of the marrow are very notably increased, the majority of the cells being of the dimensions of a large lymphocyte with pale staining nucleus of simple spherical form. The relative reduction of the granular cells of the marrow, particularly of the neutrophile variety, is sometimes a marked feature, and is most noticeable in

marrow taken from the ribs. The marrow is also frequently the seat of congestion and haemorrhages. Nucleated red corpuscles are by no means abundant, and evidences of nuclear activity in any of the types of marrow cells are very rarely met with.

Numerous examinations of the spleen-pulp, which was either withdrawn during life, or obtained shortly after death, have been carried out, the result, as regards parasites, being, as above stated, uniformly negative. The material withdrawn from the spleen-pulp during life consists almost entirely of red corpuscles with a considerable number of lymphocytes. Very few of the large mononuclear phagocytes of the spleen are found in the contents of a syringe introduced into the enlarged and indurated organ so frequently accompanying the condition. In films made post-mortem, however, the latter class of cell occurs in considerable numbers and, both in films and sections, instances of phagocytosis in this type of cell are common. The presence of considerable numbers of granular cells (eosinophiles as well as neutrophiles) which occur in post-mortem preparations of the spleen-pulp has been frequently noted, fragments of such cells being often found in the macrophages of the spleen. To a certain extent, however, the assemblage of the granular cells in the spleen-pulp may be an ante-mortem phenomenon.

Condition of the liver. The comparatively frequent occurrence of cirrhosis of the liver in various degrees, with the usual morbid changes which are associated with this condition, is a fact which soon impresses itself on the attention of any one engaged in post-mortem work in Egypt. After the exclusion of types of cirrhosis which owe their origin to alcohol, tertiary syphilis or Bilharziosis, there yet remain a very considerable majority of all the cases of cirrhosis encountered for which some other explanation must be sought. With regard to alcoholic cirrhosis, it may be said at once that its occurrence amongst a largely Moslem population is extremely rare. Tertiary syphilis also does not appear to manifest itself amongst Egyptians in the form of gumma-formation and extreme cirrhotic change in the liver so frequently as amongst Europeans, and lastly, Bilharzial cirrhosis is not only comparatively rare, but when present is so characteristic in appearance that it can be easily differentiated. An analysis of the post-mortem records of the Kasr-El-Ainy Hospital, Cairo, for the last four years reveals the presence

of cirrhosis of the liver in some degree, exclusive of the types above mentioned, in no less than 9.9 per cent. of 1,430 autopsies recorded. Of this proportion, 4.5 per cent. may be said to have died as a direct result of the secondary changes induced by cirrhosis, exhaustion after repeated recurrences of ascites being probably the most frequent cause of death. In the remainder, cirrhosis of the liver was discovered incidentally, death in these cases resulting from a great variety of other diseases. In those cases in which the disease was more or less directly responsible for death, this occurred in the large majority of cases at about thirty-five years of age. Exceptionally, however, the same changes were encountered in subjects of over sixty years of age. The most typical morbid appearances were met with in young subjects dying between the ages of seven and twenty-one years. Approximately one-third of these cases was associated with some enlargement of the liver; in the remaining two-thirds, the organ was either normal or slightly reduced in size.

The cases in which cirrhotic changes in the liver were accidentally encountered were of the most diverse character. The type of cirrhosis met with under these circumstances has been of the fine diffuse variety, and not such as to induce much, if any, external alteration of the organ. With few exceptions, there is, in these cases, a slight general enlargement of the whole organ, as well as a moderate enlargement of the spleen. Microscopically, the evidences of cirrhosis are slight, a certain amount of cellular fibrillated tissue mixed with lymphocytes surrounding groups of lobules. In a typical case seen at this stage, and undisturbed by any coincident disease, the liver cells were for the most part large, swollen and highly granular. Their nuclei, stained by the Romanowsky method, were paler than usual, and each contained several nucleoli, which, by their depth of staining, contrasted strongly with the remainder of the nucleus. Here and there, minute isolated foci of necrotic appearance, surrounded by collections of small mononuclear cells, were met with, resembling generally those seen in the liver in typhoid fever infections. Careful search made both in films and sections for parasites always yielded negative results.

In cases where death was directly attributable to the results of long-established cirrhosis, the picture presented by the liver is very different. The organ in these cases is generally reduced in size,

though never extremely so. In the majority of cases, old adhesions due to perihepatitis exist between the convexity of the liver and the diaphragm, such adhesion being sometimes complete and universal. The characters of the liver generally fulfil the picture of a multilobular cirrhosis, the nodular projections on the surface being always small, firm, and closely set. In section, the colour is generally yellow or yellowish brown, but, as in other varieties of cirrhosis, many variations in tint are often seen in the various groups of isolated lobules.

Examined microscopically, persistent islands of hepatic tissue of irregular size, mostly rounded in shape, are separated from one another by extensive bands of connective tissue of somewhat varying character. The tracts of hepatic tissue contain large, universally granular liver cells; these have lost the more or less regular ramifying arrangement in relation to lobules—indeed no definite lobules are visible even in the largest persistent tracts.

The liver cells vary considerably in size, the larger frequently containing two nuclei, as if compensatory hepatic regeneration is in progress. The liver cells are frequently vacuolated or show other signs of degeneration than the granular character already mentioned. They sometimes exhibit a very marked 'vesicular' degeneration. In such areas, the hepatic cell nuclei are reduced in number, and those which persist, stain more faintly than is the rule elsewhere. The cells referred to have not a definitely fatty appearance, but suggest that degeneration products of the protoplasm have been dissolved out in great part, leaving only a hazy, reticulated residuum. The tracts of connective tissue separating the hepatic islands are densely cellular. Between the connective tissue fibrillae are multitudes of small lymphocytes. Polymorphonuclear cells, some of which are eosinophilous, occur fairly frequently amongst them. In these tracts, hepatic cells, single or in small groups, are found, showing pressure and other changes. Considerable numbers of small capillary vessels, with thin walls, are also found in these tracts. Where the lymphocytic infiltration is less dense, one sees that spindle-shaped fibroblastic elements largely compose the tissue. There is a comparative absence of the increased duct formation common in other varieties of hepatic cirrhosis.

Condition of the spleen. In the entire series of cases under consideration, enlargement of the spleen is the result. While splenic enlargement from other causes is of course frequently met with, it may be affirmed generally that distinct and sometimes great enlargement of the spleen is more regularly associated, in Egypt, with cirrhosis of the liver than with conditions unconnected primarily with this organ. As might be anticipated, the greatest degree of enlargement is found in cases where the cirrhosis is of the more advanced and contracted type just described. In several such cases, the weight of the spleen has been between 1,000 and 1,250 grammes, and in one case (that of a girl aet. fourteen with advanced cirrhosis) the weights of the liver and spleen were identical, viz., 1,450 grammes. Apart from such exceptional instances, however, the average weight of the organ has been found to be 450 grammes.

In consistence, the spleen is firm, frequently, indeed, quite hard, and presents a uniformly and deeply congested pulp in which the Malpighian bodies are generally only detected with difficulty.

Apart from the facts already stated in connection with the examination of the splenic tissue in films stained by the Giemsa or Romanowsky methods, the examination of sections of splenic tissue has yielded few results of any significance.

These may be summarised as follows:—

- (1) Hyperplasia of the lymphocytic elements of the pulp.
- (2) General increase of the connective tissue. This occurs either in the form of a definite increase of the compact fibrous trabeculae of the organ, or, in the case of the larger spleens, as an infiltration of spindle-shaped cells diffusely distributed throughout the entire pulp.
- (3) Distension and congestion of the vascular sinuses and frequent interstitial haemorrhages.
- (4) Active phagocytosis on the part of the macrophages towards red corpuscles and leucocytes. The occurrence of intracellular pigment from the former source, is commonly noted.

Condition of the intestine. In view of the lesions reported in the intestine in cases of Kala-Azar, the condition of the bowel has always been carefully scrutinised. It is not possible, however, in our opinion, to uphold the association of any definite lesion of the intestine with the condition in question, notwithstanding the clinical fact that

intestinal symptoms are very commonly a feature of the disease in the earlier part of its course. The intestine, in about a quarter of the cases examined, has presented various lesions. Some of these had all the characters of dysenteric ulceration either in an active or chronic form. Others showed an enterocolitis, affecting principally the lower part of the ileum and the entire colon, the inflamed surface being covered with a thin, irregular membranous exudation. In a few cases, multiple small oval ulcers of the colon were present. Their longer axes, generally less than one cm. in length, were transverse to the long axis of the bowel, and their edges were slightly raised, soft and crateriform. Microscopical examination of such lesions has, so far, yielded negative results, as regards the presence in them of any unusual parasites.

CRITICAL SUMMARY

Whatever the ultimate explanation of the condition dealt with in this paper may be, we feel that it constitutes a clinical and pathological entity the result of some infective agent of which we are as yet ignorant. The possibility that either Bilharziosis or Ankylostomiasis can have any causal relationship with this disease cannot, in the light of our statistical, clinical and pathological evidence, be admitted. Bearing in mind the condition of the blood and bone-marrow which characterises the disease, the deduction seems reasonable that, if it be produced by an infective agent, this is more likely to be found of protozoan than bacterial nature. In this connection, the recent discovery by one of us (A. R. F.) of large numbers of a parasite having the closest resemblance to that of Kala-Azar, and probably identical with that found in the Delhi Sore and Aleppo Boil, occurring in ulcerated papillomatous lesions on the limbs of Egyptian fellaheen, is not without significance. Dr. Bitter, Bacteriologist to the Government Department of Public Health, Cairo, has also found similar bodies in a lesion of this nature. It must be borne in mind, further, that our numerous attempts to find parasites in the internal organs have generally been carried out on patients already far advanced in the disease. Kala-Azar, while closely resembling the condition which we have described in certain respects, differs from it in others. Thus, the febrile onset, chronic course, presence of

intestinal symptoms, the aspect of the patient in the advanced stages, the condition of the blood, bone-marrow and spleen, are very closely similar in both affections. Kala-Azar, however, in the following particulars, apart from certain clinical features, differs from the condition to which we have called attention:—

(1) The presence of a crusted papular eruption or of ulcers on the limbs, containing the parasite.

(2) The presence of intestinal ulcers, chiefly in the colon, also containing the parasite in small numbers.

(3) The tendency to noma and local areas of gangrene, as well as to internal haemorrhages.

(4) The condition of the liver. In sporadic Kala-Azar, according to Rogers' observations, the liver showed marked cirrhotic changes in four out of forty-eight cases examined post-mortem, while slight degrees of fibrosis were observed in a certain additional number. In the condition we are describing, however, hepatic changes in various degrees form an integral part of the malady at different stages, and are constantly met with. Again, the type of cirrhosis met with is portal in character and not intralobular, as described by Rogers for Kala-Azar. And lastly, 'the persistence of the parasites in the advanced cirrhotic stage of the organ,' as noted by Rogers in Kala-Azar, is a feature which stamps a distinctive character on the liver in this affection.

For several reasons also we are unable to accept the view that chronic malaria can be held responsible for this class of case. The comparative rarity of malaria in Cairo may be gauged from the fact that not more than one or two cases are seen at hospital in the course of a year. Further, in the small proportion of cases of splenomegaly and cirrhosis accompanied by distinct fever there were no recurrent paroxysms, nor was the condition ameliorated by even considerable doses of quinine. Other reasons, founded on the pathological appearances, are the following:—

(1) The entire absence of any signs of malaria parasites (particularly the 'gametes' of former aestivo-autumnal infections) in our numerous examinations of the blood, and more particularly, of the spleen-pulp, in these cases.

(2) The absence of pigmented leucocytes in the circulation or in the viscera.

(3) The absence of visceral pigmentation in those situations commonly so affected in malaria.

(4) The character of the changes in the bone-marrow.

(5) The advanced degree and coarse character of the cirrhotic changes in the liver. It is, in our opinion, extremely doubtful whether malaria *of itself*, however severe or prolonged, can give rise to such pronounced cirrhotic change.

The differentiation of this disease from, or the determination of its possible relationship with, other forms of splenomegaly, such as chronic splenic anaemia, Banti's disease, and that found in marasmic infants suffering from gastro-enteritis, presents very considerable difficulties. To these, and closely allied to the last form, must be added a very similar but incompletely investigated condition, known under the name of 'Ponos,' and met with in certain islands of the Greek Archipelago.

That all these conditions, including that with which we have to deal in Egypt are referable to intestinal infection or toxaemia, is in the highest degree probable; and the view, so frequently urged by Continental writers, that certain of them (*viz.*, the splenomegaly of marasmic infants, chronic splenic anaemia, and Banti's disease) may all represent chronologically different stages of essentially the same disease, may ultimately be found to be true. But, until the essential identity and continuity of this prolonged process has been more regularly and constantly established, it appears necessary to retain the name 'chronic splenic anaemia' for what must be regarded, from the point of view of this hypothesis, as the intermediate stage of the process.

The condition which we describe is thus seen to differentiate itself at once from splenic anaemia by the regular coincidence of hepatic changes which, up to a certain stage, advance, *pari passu*, with those in the spleen, and taking the lead in the later stages, become largely responsible for the train of events leading to a fatal issue.

There remains the question of its identity with, or relation to, Banti's disease. It may at once be said that the existing records of the latter disease—comparatively restricted in number—do not permit of any differentiation between the two conditions. For the present, therefore, we may be content to remark that, closely comparable, if